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Lidocaine 5%–medicated plaster (Versatis) for localised neuropathic pain: results of a multicentre evaluation of use in children and adolescents

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Abstract

The Lidocaine 5% plaster is licensed for the symptomatic relief of neuropathic pain associated with post-herpetic neuralgia in adult patients over 18 years of age. Studies in adults also demonstrate efficacy of Lidocaine 5% plasters in other neuropathic pain conditions. Case reports and experience suggested efficacy of Lidocaine 5% plasters in children and adolescents with localised neuropathic pain. Initiated by the Pain in Children Special Interest Group (PICSIG) of the British Pain Society, a 3-year prospective multicentre service evaluation was undertaken to document the usage and efficacy of the Lidocaine 5% plaster in paediatric patients being managed by paediatric pain teams in the United Kingdom. Five paediatric pain teams provided anonymised data pre-treatment and 3–6 months after commencing Lidocaine 5% plaster. Changes in pain score, function, sleep and continuing use were evaluated. Data were obtained for 115 patients; age range 5–18 years (mean: 12 years). Diagnosis and site of application varied. Benefit from use of a Lidocaine 5% plaster in an individual was deemed if two or more of the following were reported: reduction in pain score, functional improvement, sleep improvement and continuing use of Lidocaine 5% plaster. Benefit was recorded for 79 patients (69%); 32 patients were recorded as receiving no benefit and data were unavailable for 4 patients, and 7 patients reported minor skin reactions. This prospective service evaluation supports the efficacy of the Lidocaine 5% plaster in children and adolescents with localised neuropathic pain and confirms tolerability and safety. It is the opinion of the PICSIG of the British Pain Society that the Lidocaine 5% plaster should be considered early in the multidisciplinary management of localised neuropathic pain in children and adolescents.

Keywords

Lidocaine, neuropathic pain, child, school child, adolescent, lidocaine patch, lidocaine plaster, Versatis

Introduction

Chronic neuropathic pain in children and young people results from a variety of medical conditions, for example, trauma, infection, surgery and cancer.[1] Neuropathic pain frequently causes great distress and compromises quality of life and often responds poorly to standard analgesics. Adjuvant analgesics such as

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Table 1. Diagnoses of localised neuropathic pain.

ICD 11 diagnosis	Sub-type	Number
Chronic neuropathic pain	Chronic peripheral neuropathic pain (e.g. neurofibromatosis, post-herpetic neuralgia and Erb's palsy)	8
	Chronic central neuropathic pain (e.g. syrinx and Spina bifida)	6
Chronic post-surgical pain	Peripheral neuropathic pain	30
Chronic post-traumatic pain	Peripheral neuropathic pain	5
Chronic primary pain	Complex regional pain syndrome Type 1	22
	Chronic musculoskeletal back pain with neuropathic features	15
	Chronic musculoskeletal chest pain with neuropathic features	7
	Chronic visceral pain with neuropathic features	5
	Chronic peripheral pain with neuropathic features	12
	Other	5

ICD 11: eleventh revision of the International Classification of Diseases.

antidepressants and antiepileptics are often effective but tolerability is frequently a problem due to unpleasant side effects. Recent Cochrane reviews found no evidence to support or refute the use of antidepressant or antiepileptic drugs to treat chronic non-cancer pain in children and adolescents.[2,3]

Lidocaine is a local anaesthetic which reversibly inhibits conduction of neuronal impulses by blocking sodium channels and stabilising neuronal membranes. The hydrogel plaster also protects the hypersensitive area. The safety and tolerability of the Lidocaine 5% plaster (Versatis) is established and licensed for the symptomatic relief of neuropathic pain associated with post-herpetic neuralgia in adult patients over 18 years of age. Studies in adults have also demonstrated efficacy of Lidocaine 5% plasters in other neuropathic pain conditions, particularly diabetic peripheral neuropathy.[4] Reports of use in children and adolescents are favourable, but all are case reports other than one study in 14 paediatric burn patients with neuropathic pain.[5]

Based on published case reports and experience of its members, the Pain in Children Special Interest Group (PICSIG) of the British Pain Society determined to perform a prospective multicentre service evaluation to document the usage and efficacy of the Lidocaine 5% plaster in paediatric patients being managed by paediatric pain teams in the United Kingdom.

Method

A 3-year prospective service evaluation was initiated by the PICSIG supported by an unrestricted educational grant from Grunenthal. Coordination of the project was at Sheffield Children's Hospital, where the service evaluation was registered with the Trust's clinical audit and effectiveness department: ethical approval was not required. The database was registered with the Healthcare Quality Improvement Partnership. Invitations to take part, along with questionnaires to be used, were distributed to 13 paediatric pain teams across the United Kingdom. Anonymous pre-treatment data included the following: age, sex, weight, duration, location and type of pain, diagnosis, pain score (numerical rating scale 0–10), current medication, previous medication, application site and duration and timing of planned application. Similar follow-up data were collected approximately 3–6 months post treatment. In addition, enquiry was made regarding side effects, continued or discontinued use of the plaster and families self-rating of effect on physical functioning and sleep.

Results

Five centres participated in the service evaluation. Data from 115 sets of questionnaires collected from October 2010 to September 2013 are presented; 81 females and 34 males are included with ages ranging from 5 to 18 years (mean 12 years). Several pain descriptors were reported, the most common being shooting or stabbing pain and hypersensitivity. Diagnoses for pain are presented in Table 1: the two most common being post-surgical peripheral neuropathic pain and complex regional pain syndrome type 1. Duration of pain prior to commencement of plaster use was between 1 month and 14 years (mean 23 months). Plaster use was recommended for 12 continuous hours in a 24-h period, either during the day or at night: the majority of patients used the plaster during the day. Most patients used one plaster; 4 patients used 2 plasters and 16 used less than one plaster. Current and previous medication included simple analgesics, opioids, amitriptyline, gabapentinoids, ketamine and clonidine.

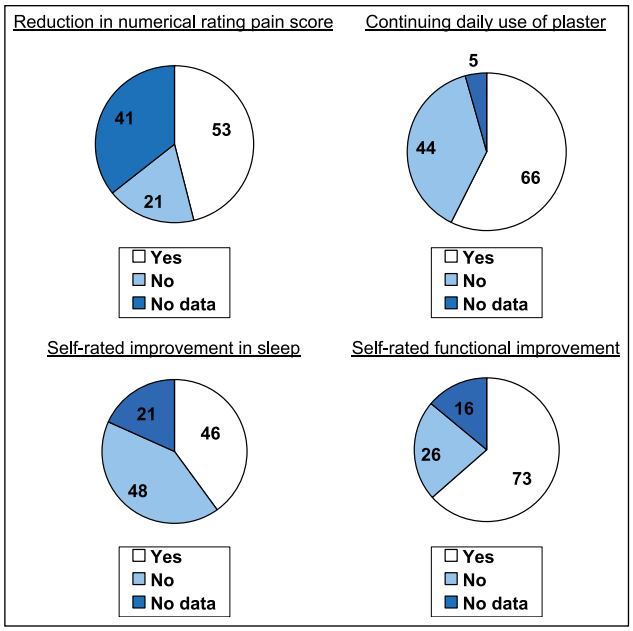

Figure 1. Outcome measures in 115 children and adolescents.

Benefit from the Lidocaine 5% plaster was deemed if two or more of the following four criteria were met at follow-up:

1. Self-rated functional improvement;
2. Self-rated improvement in sleep;
3. Reduction in numerical rating pain score;
4. Continuing daily use of plaster.

A total of 79 (69%) patients received benefit, 32 had no benefit and data were incomplete for 4 patients. Figure 1 provides further detail on benefit. No patient reported receiving benefit purely on improved sleep and continuing daily use of the plaster alone. For those who did not benefit, most did not like applying the plaster over the painful area or found that the plaster did not adhere well to the skin, especially in warm weather.

Seven patients (6%) reported skin reactions to the plaster; four of these discontinued the plaster.

Discussion

The first published reports of the use of the Lidocaine 5% plaster in a child were in 2002 for erythromelalgia[6] and in 2003 for complex regional pain syndrome Type 1;[7] both patients gained benefit. Four of five children with post-surgical neuropathic pain were reported in 2008 to benefit from using the plaster.[8] Further benefit was reported in 2013 in six children with sickle cell disease[9] and in 2017 in three children with epidermolysis bullosa.[10] In 2013, a prospective study of 14 paediatric patients with neuropathic pain from burns sequelae reported benefit in all 12 available for follow-up and also reported low levels of plasma lidocaine.[5]

The early case reports, combined with anecdotal experience of members of the PICSIG, stimulated us to undertake a prospective national service evaluation. The heterogeneity of localised neuropathic pain in children mitigates against a prospective controlled trial, and pragmatically, it was felt that reasonable numbers would only be available by a service evaluation approach. It was disappointing that only 5 of 13 centres chose to participate. We accept that the heterogeneity of patients, concurrent use of other pharmacological and non-pharmacological management and the use of qualitative outcome measures all dilute the conclusions that can be drawn from this evaluation. If the local coordinator was not present at the follow-up clinic consultation, the questionnaire was filled in by them after the clinic using the clinical notes, resulting in some loss of data for outcome measures. Nonetheless, perceived benefit in 69% of 115 children and adolescents, with no serious side effects, suggests clinical utility in a condition for which there is no evidence-based treatment. A global judgement of improvement and satisfaction, as recommended by PedIMMPACT, was not included in the questionnaire: it would probably have been helpful. Continuing daily use of the plaster in 57% of patients, with minimal side effects, is perhaps a surrogate indicator of global satisfaction. The plasters were well tolerated in most patients; pain on application and removal and poor adherence in warm weather accounted for discontinued use in many cases. Being able to cut the plaster to size, without affecting drug delivery, is very helpful in paediatric patients and for distal application to limbs.

A Cochrane review on topical lidocaine for neuropathic pain in adults in 2014[11] concluded that there was no evidence from good-quality randomised controlled studies to support the use of topical lidocaine to treat neuropathic pain, although individual studies indicated that it was effective for relief of pain. The latest NICE guideline on the pharmacological management of neuropathic pain in adults in non-specialist settings[12] does not recommend topical lidocaine, but does make a research recommendation to further investigate the use of this treatment for localised peripheral pain because it could be a potential alternative treatment for people who do not wish to, or are unable to, take oral medications. Nonetheless, for economic reasons, the NHS considers Lidocaine 5% plasters to be of low priority[13] and seeks to restrict their prescription in primary care.[14] In contrast, authoritative international guidelines recommend the Lidocaine 5% plaster as first-line[15] or second-line[16] treatment, particularly in the elderly. A recent international review

on the place of the Lidocaine 5% plaster in guidelines suggests that it should be more strongly recommended based on tolerability and safety and long-term efficacy.[17] The dichotomy of views is primarily related to cost and economic analyses. Interestingly, a recent Brazilian cost-effectiveness analysis was very favourable for the Lidocaine 5% plaster when compared to gabapentin and pregabalin.[18]

In children and adolescents, there is no evidence base for the systemic treatment of localised neuropathic pain and there are no guidelines. Furthermore, adverse effects of antidepressant and antiepileptic medicines, particularly cognitive effects, strongly favour use of topical treatments when the most important goal is usually enabling regular school attendance. This prospective service evaluation supports the efficacy of the Lidocaine 5% plaster in children and adolescents with localised neuropathic pain. The plaster should be applied over the painful area; there are no published data to guide the number of plasters in children, but plasma levels were many times lower than toxic levels in the only paediatric data available[5] in keeping with adult data. Pragmatically, we recommend a maximum of up to one plaster if <30kg, up to two plasters if 30–60 kg and up to three plasters if >60kg. Lidocaine 5% plasters are relatively expensive; however, the economic costs of chronic pain in adolescence are also high; in 2005, a preliminary study estimated the annual cost of illness to be £3840 million in the United Kingdom.[19] We accept that concurrent use of other pharmacological and non-pharmacological management, and the use of non-validated qualitative outcome measures, dilutes the conclusions that can be drawn from this evaluation. Nonetheless, it is the opinion of the PICSIG of the British Pain Society, supported by this prospective service evaluation, that the tolerability and safety of the Lidocaine 5% plaster, combined with a reluctance to prescribe long-term antidepressant or antiepileptic medication to children and adolescents, favour the early use of Lidocaine 5% plasters for localised neuropathic pain when part of a multidisciplinary pain approach.

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Conflict of interest

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